

PATENT COOPERATION TREATY

REC'D 0.8 AUG 2005

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From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
MERCK & CO., INC.  
126 EAST LINCOLN AVENUE  
RAHWAY, NJ 07065-0907

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) 04 AUG 2005

Applicant's or agent's file reference

FOR FURTHER ACTION

See paragraph 2 below

PCT 21622Y

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US05/40153

25 March 2005 (25.03.2005)

29 March 2004 (29.03.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 31/535, 31/497, 31/4965; C07D 401/00, 403/00, 405/00, 409/00, 411/00, 413/00, 417/00, 419/00, and US Cl.:  
514/235.8, 252.1, 252.11, 255.05; 544/120, 333, 405, 408

Applicant

MERCK & CO., INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US  
Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (703) 305-3230

Authorized officer

Zachary C. Tucker

Telephone No. (571) 272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/10153

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US05/10153

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims 1-52 YES  
Claims NONE NO

Inventive step (IS)

Claims 1-52 YES  
Claims NONE NO

Industrial applicability (IA)

Claims 1-52 YES  
Claims NONE NO

2. Citations and explanations:

Claims 1-52 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest any compound, composition or method as are instantly claimed.

The closest prior art with respect the compounds of the invention comes from HIRANO et al, "Reaction of Pyrazinium Ion Having Aryl and Cyano Groups with Hydride Reagents or Hydroxide Ion" Journal of Heterocyclic Chemistry, vol. 18, pages 905-908 (August 1981). Page 906 includes reaction diagrams showing formation of compound IX. The accompanying commentary in the column directly above this diagram, the reference states that the hydrolysis product of compound IX is also formed. Hydrolysis product of IX is 3-carbamoyl-5-(3,4-dimethoxyphenyl)-1-methyl-1,6-dihydropyrazine-6-one, which is a compound similar to claim 1 compounds, but lacking a phenyl substitution on the phenyl ring bound to the pyrazinone ring.

No prior art disclosing compounds according to the instant claims was found in a search.

Claims 1-52 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in the pharmaceutical and medical industries.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US05/10153

**Box No. VIII Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Structural formulae depicted in claims 1 and 4-7 are incorrect - the carbon to which the carbonyl oxygen is bound on the pyrazinone ring is pentavalent, which is an impossible bonding arrangement. The claims have been searched as if the proper bonding in the pyrazinone ring were shown.

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-52</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>1-52</u>	YES
	Claims <u>NONE</u>	NO
Industrial applicability (IA)	Claims <u>1-52</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

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